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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/681,142 | 10/09/2003 | J. Michael Ramstack | 000166.0073-US02 | 6453 |

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COVINGTON & BURLING
ATTN: PATENT DOCKETING
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WASHINGTON, DC 20004-2401

| EXAMINER | |
|---|---|
| BERKO, RETFORD O | |
| **ART UNIT** | **PAPER NUMBER** |
| 1615 | |

DATE MAILED: 12/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/681,142 | RAMSTACK ET AL. | |
| | Examiner | Art Unit | |
| | Retford Berko | 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *18 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## *DETAILED ACTION*

**Acknowledgement**: The Information Disclosure Statement filed February 18, 2004 is acknowledged.

### Status of Claims

Claims 1-34 are pending in this application in view of Applicant's amendment.

### Joint Inventors

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

### Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Instant claims 1, 2, 5, 6, 8, 11, 13; and 20-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Patented claims 49, 22-26; 50, 51, 52, 42, 39 (method claims) and claims 1, 17, and 35 of US Patent No. 6, 495, 164 to Ramstack et al; in view of Herbert et (US 5, 654, 008).

The instant claims are directed toward a method for preparing a composition in the form of microparticles suitable for injection through a host; said method comprising the steps of (a) mixing dry microparticles to form a suspension and (b) mixing the suspension with a viscousity-enhancing agent in order to achieve specified viscosity that is injectable through a needle of a specified diameter gauge. The claims are also directed toward the composition comprising of suitable pharmaceutically active agents (e.g. risperidone or its derivative) and also towards a method of administering the suspension containing the active agent to the host.

Ramstack et al (US 6, 495, 164) is a co-inventor of the claims currently under review. As in the instant claims, Patent '164 teaches a method of making a composition (risperidone or 9-hydroxyrisperidone) suitable for injection through a needle, said method comprising (a) mixing dry microparticles with an aqueous injection vehicle that comprises a viscosity-enhancing agent to form a suspension; (b) removing water from the suspension and (c) resconstituting with solvent to obtain an injectable suspension. Ramstack (Patent '164) teaches the use of viscosity enhancing agent (col 20, lin 1-5). Patent '164 does not teach how to obtain microparticles containing a high concentration of the active agent for injection.

Herbert et al, US Patent No 5, 654, 008; col 12, lin 8-20, lin 45-55) teach method of making microparticles comprising risperidone. It would have been obvious to one of ordinary skill to prepare microparticles by modifying the method of Herbert et al, ie. changing the

conditions of preparation such as mixing (use of static mixture), solvents and other ingredients in order to obtain the advantage of high quality microparticles having high concentration of active agents for injection into a host (as in Herbert et al, US Patent No 5, 654, 008; col 12, lin 8-20, lin 45-55).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-10, 33, 34, 20, 22-28 and 31 are rejected as unpatentable under 35 U.S.C. 103(a) over Tice et al (US 6, 306, 425; filed April 7, 2000).

The claims are directed toward a method of preparing a composition in the form of microparticles, suitable for injection to a host, said method comprising the steps of (a) mixing

dry microparticles to form a suspension and (b) mixing the suspension with a viscousity-enhancing agent in order to achieve specified viscosity that is injectable through a needle of a specified diameter gauge. The claims are also directed toward the suspension having specified viscosity (20 cp to 600 cp at 20 degrees) and suitable for injection through a needle having a diameter of 18-22 gauge. The claims are further drawn toward the composition comprising of suitable pharmaceutically active agents (e.g. risperidone or its derivative), a polymeric binder (d,l-lactide or copolymer poly-d,l-lactide-co-glycolide) and sodium carboxymethyl cellulose as viscosity enhancing agent.

Tice et al (Patent '425) discloses a method of making naltrexone in poly(D,L-lactide) matric in the form of microspheres suitable for passing through syringe needle for injection into a host (abstract). A detailed, step-wise method is provided as how to make the microcapsule suspension (col 7, lin 5-50 and col 19, lin 5-25). According to Tice, the matrix has an inherent viscosity in view of the polymer (col 3, lin 40-55), that a combination of polymers can be applied in amounts to adjuct the viscosity of the composition (col 3, lin 55-65) and the method describes the use of viscosity-enhancing agent---e.g. carboxymethyl cellulose and mannitol (col 4, lin 40-60). Patent '425 discloses the use of a 18-gauge needle for administration of the suspension containing microspheres to a host (col 8, lin 35-65).

Patent '425 does not specifically teach the use of viscosity-enhancing agent in the second solvent that allows an increase in the viscosity to achieve a range of 20 cp to 600 cp at 20 degrees.

One of ordinary skill in the art would be motivated to prepare microspheres comprising active agents and polymers carboxymethyl cellulose as viscosity enhancing agents and modify

the amounts of polymer in order to achieve the desirable increased viscosity. By varying the amounts of viscosity-enhancing agent and modifying additives such as mannitol, buffer and detergents; one of ordinary skill would expect to achieve increased viscosity and in addition, retain an advantage of diminishing the discomfort from injection of the microspheres when used in multiple injections and enhanced levels of active agent while as disclosed by Tice et al (col 4, lin 40-50 and col 6, lin 20-35). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill at the time it was made.

2. Claims 1-10, 33, 34 (method); 20, 22-28, 31 (composition) and (11-19, 21 and 32 (method of administering) are rejected as unpatentable under 35 U.S.C. 103(a) over Tice et al (US 6, 306, 425) in view of Hutchinson et al (US 6, 034, 175; filed Jan 22, 1999)

The claims are directed toward a method of preparing a composition in the form of microparticles, suitable for injection to a host, said method comprising the steps of (a) mixing dry microparticles to form a suspension and (b) mixing the suspension with a viscousity-enhancing agent in order to achieve specified viscosity that is injectable through a needle of a specified diameter gauge. The claims are also directed toward the suspension having specified viscosity (20 cp to 600 cp at 20 degrees) and suitable for injection through a needle having a diameter of 18-22 gauge. The claims are further drawn toward the composition comprising of suitable pharmaceutically active agents (e.g. risperidone or its derivative), a polymeric binder (d,l-lactide or copolymer poly-d,l-lactide-co-glycolide) and sodium carboxymethyl cellulose as viscosity enhancing agent. The claims are also drawn to method of administering the composition to a host.

The disclosures of Tice et al (Patent '425) have been discussed. Patent '425 does not specifically teach the use of viscosity-enhancing agent in the second solvent that allows an increase in the viscosity to achieve a range of 20 cp to 600 cp at 20 neither does

Hutchinson et al (Patent '175) disclose a method of making microparticles of active agents suspended in aqueous injection vehicles (col 13, lin 10-20; col 17, lin 40-40 and col 31, lin 15-35; col 34, lin 65, continuing to col 35 and col 45, lin 35-45). Patent '175 disclosed the viscosity of suspension and also disclosed the method of administering the suspension to a host (col 31, lin 15-35). According to the method disclosed in Huchinson, the use of sodium carboxymethyl cellulose (medium viscosity grade and carriers such as methyl cellulose and polysorbate 80 were suitable carriers for parenteral administration (col 35, lin 1-5).

One of ordinary skill in the art would be motivated to prepare microspheres comprising active agents and polymers carboxymethyl cellulose as viscosity enhancing agents and modify the amounts of polymer in order to achieve the desirable increased viscosity. By varying the amounts of viscosity-enhancing agent and modifying additives such as mannitol, buffer and detergents; one of ordinary skill would expect to achieve increased viscosity and in addition, retain an advantage of diminishing the discomfort from injection of the microspheres when used in multiple injections and enhanced levels of active agent while as disclosed by Tice et al (col 4, lin 40-50 and col 6, lin 20-35). Moreover, one of ordinary skill in the art would expect to gain additional advantage of applying the method toward preparation of readily injectable peptide drugs that are otherwise ordinarily difficult to administer by injection to patients (Patent '175, col 17, lin 18-25 and col 18, lin 12-25). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill at the time it was made.

**Correspondence**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Retford Berko** whose telephone number is571-272-0590. The examiner can normally be reached on M-F from 8.00 am to 5.30 pm

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Thurman K Page**, can be reached on 571-272-0602.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RoB
12/16/04

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